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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GROSS, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,882	MCGREGOR, DUNCAN	
	Examiner	Art Unit	
	Christopher M. Gross	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,3-7,9 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Responsive to communications inserted 3/30/2006. Examiner on instant case has changed (see contact information below). Claims 1,3-7,9,24-26 are pending. Claims 1,3-7,9,24-26 are examined herein.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/27/2006 has been entered.

Priority

This application is a 371 of PCT/GB98/02630, which claims priority to UK application 9718455.0, filed 9/2/1997.

Receipt is again acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Withdrawn Rejections

Applicant's arguments, see pp 2-3, filed 3/30/2006, with respect to the new matter issue under 35 USC 132, raised in the advisory action (IFW date 3/2/2006), have been fully considered and are persuasive. The new matter issue raised in the advisory action has been reconsidered.

Applicant's arguments, see pp 7-10, filed 1/27/2006, with respect to the rejection(s) of claim(s) 1,3-6,8-10 and 25 under 35 USC 102(b) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.

Applicant's arguments, see pp 10-11, filed 1/27/2006, with respect to the rejection(s) of claim(s) 1,3-10 and 24-26 under 35 USC 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.

Upon further consideration, however, a new ground(s) of rejection is(are) made in view of the amendments to the claims on 1/27/2006 (see below).

New Claim Rejections - 35 USC § 112

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3-7,9,24-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention is broadly drawn to a "peptide display carrier package" (PDCP) comprising a *nuclear steroid receptor* chimeric fusion protein plus a *single stranded polynucleotide* comprising a specific recognition sequence motif for said nuclear steroid receptor chimera.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, by disclosure of relevant, identifying characteristics (i.e., structure or other physical and/or chemical properties), by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly 119 F.3d at 1568. 43 USPQ2d at 1406.

The specification does not describe a representative number of species in the genus of nuclear steroid receptors capable of binding *single stranded* polynucleotides. With the exception of the estrogen receptor, disclosed on pp 19-20 of the specification, the skilled artisan cannot immediately envision which other species in the genus of nuclear steroid receptors (e.g. glucocorticoid, vitamin A, vitamin D, etc.) would be capable of binding single stranded DNA, and thus be included as part of the claimed genus.

Therefore, only the genus of nuclear steroid receptors consisting of the estrogen receptor, rather than the full breadth of the claim meets the written description provision

of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1,3-7,9,24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the species of chimeric fusion proteins comprising the estrogen receptor, it does not reasonably provide enablement for the genus of nuclear steroid receptors capable of binding single stranded DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether undue experiment is necessitated. These factors can include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the relative skill of those in the art;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1 and 2) The breadth of the claims and the nature of the invention: The invention is broadly drawn to a PDCP comprising a *nuclear steroid receptor* chimeric fusion protein plus a *single stranded polynucleotide* comprising a specific recognition motif (sequence) for said nuclear steroid receptor chimera.

(3 and 5) The state of the prior art and the level of predictability in the art: The binding preference (ssDNA vs. dsDNA) of nuclear steroid receptors is unpredictable. Moreover, ssDNA binding is more the exception than the rule: for efficient binding, most nuclear steroid receptors exist in solution as dimers and require the presence of geometric symmetry, a minor and major groove, etc., all of which is provided in dsDNA (see for example, Gearhart, et al 2005 Biochemistry 44:4196-4203, figure 1). Prediction of a particular ssDNA sequence with high affinity for a given nuclear steroid receptor proteins is not yet possible in the art.

(4) The level of one or ordinary skill: The level of skill would be high, most likely at the Ph.D. level or equivalent number of years experience. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

(6 and 7) The amount of direction provided by the inventor and the existence of working examples: Applicant teaches one example of the estrogen receptor capable of binding ssDNA. Said example is not generalizable, as nuclear steroid receptors are usually not known to bind ssDNA. Applicant does not provide protocols for discerning the requisite ssDNA sequence capable of binding other nuclear steroid receptor besides estrogen receptor.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: As the disclosed specification does not provide protocols for discerning the requisite ssDNA sequence capable of binding nuclear steroid receptors, the amount of experimentation necessary is substantial since predicting a ssDNA sequence capable of binding a given nuclear steroid receptor remains a challenge in the art. The procedure followed for the estrogen receptor is not applicable toward other nuclear steroid receptors. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, undue experimentation would be required of one of skill in the art to practice the full scope of the claimed invention.

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,4-7,9,24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments, pp 3-5, filed 3/30/2006, concerning the amended language, "...polynucleotide is protected from degradation by a binding moiety which is a protein and which is bound non-specifically to the polynucleotide..." being definite, since the specification teaches embodiments describing the binding proteins is not found persuasive because the limitation is not explicitly stated in the claim.

According to MPEP 2111, quoting *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969): "reading a claim in light of the specification, to thereby interpret limitations explicitly recited in the claim, is a quite different thing from reading limitations of the specification into a claim,' to thereby narrow the scope of the claim by implicitly adding disclosed limitations which have no express basis in the claim." Emphasis added.

The limitation that the polynucleotide is protected by a phage coat protein is not explicitly reflected in the claims, thus the claims read on any protein, including the chimera, and are indefinite. As currently written, the metes and bounds of the claims are unascertainable.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1,3-7,9,24-26 rejected under 35 U.S.C. 103(a) as being unpatentable over **Rebar et al** (1994 Science 263:671-673) in view of **Lannigan et al** (1989 PNAS 86:863-867).

The claimed invention is drawn to a synthetic construct which is a PDCP, said construct comprising a complex of a recombinant single-stranded polynucleotide and a chimeric protein, wherein

(i) the chimeric protein has

(a) a nucleotide binding portion which comprises a binding domain of a nuclear steroid receptor; and

(b) a target peptide portion displayed externally on the package, and

(ii) said recombinant polynucleotide comprises

(a) a chimeric protein-encoding portion which encodes the chimeric protein of the complex; and

(b) a nucleotide sequence motif which is specifically bound by said nucleotide binding portion of the chimeric protein,

and wherein the nucleotide binding portion of the chimeric protein is bound to the nucleotide sequence motif of the recombinant polynucleotide, and wherein the chimeric protein-encoding portion of the recombinant polynucleotide is not bound by the nucleotide binding portion of the chimeric protein, and wherein the chimeric protein-encoding portion of the recombinant polynucleotide is protected from degradation by a binding moiety which is a protein and which is bound non-specifically to the polynucleotide irrespective of nucleotide sequence and wherein said construct is produced in a host cell transformed with said recombinant polynucleotide and extruded therefrom without lysis of the host cell. Claims 3-7,9,24-26 represent variations thereof.

Rebar, et al teach, throughout the document and especially the abstract and figure 1, a phage display system for affinity selection of zinc fingers with new DNA binding affinities. Said phage display system of Rebar et al comprises a PIII-tri-zinc finger fusion protein and is taken to be the PDCP, single stranded polynucleotide and chimeric protein of the preamble of claims 1, 24 and 25, the 'nucleotide binding portion' of part (i) (a) of claims 1, 24 and 25, the entirety of part (ii) (a) of claim 1 and the

'chimeric protein-encoding portion which encodes the chimeric protein of the complex' of claims 24 and 25.

Rebar et al teach DNA binding assays with recovered phage particles and thus the PIII-tri-zinc finger is displayed externally on the particle, is taken to be the '[external] display' of claim 24 and part (ii) (b) of claim 1 and claim 4. The phage DNA of Rebar et al are extruded from the bacterial cell, protected with phage coat proteins, which is taken to provide the 'the recombinant polynucleotide is protected from degradation by a binding moiety which is a protein and which is bound non-specifically to the polynucleotide irrespective of nucleotide sequence and wherein said construct is produced in a host cell transformed with said recombinant polynucleotide' of claims 1 and 25, the 'binding moiety is a viral coat protein' of claims 3, 24 and 26 as well as the 'extruded therefrom without lysis of the host cell' of claims 1 and 25.

Rebar et al teach in the legend to figure 1A, the insertion of a polylinker into the phage vector, which is taken to be the linker sequence of claims 5 and 24. Rebar et al teach the tri-zinc finger protein encoding sequence is inserted at the N terminal of the PIII sequence, which is taken to be the N terminal of claim 9 and 25.

Rebar et al do not teach a nuclear steroid receptor fusion protein - capable of binding single stranded DNA - or its DNA recognition sequence, however.

Lannigan et al teach, throughout the document, and especially figure 4 the estrogen receptor preferentially binds the coding strand (i.e. ssDNA) of the estrogen response element (ERE) and the former is taken to be the oestrogen receptor of claims

7 and 24. In figure 1, Lannigan et al further teach multiple EREs on a stretch of DNA, which is taken to be two of more nucleotide sequence motifs of claim 6.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to use the coding strand and estrogen receptor of Lannigan et al with the phage display system of Rebar et al.

One of ordinary skill in the art would have been motivated to use the estrogen receptor and ERE coding strand of Lannigan et al with the phage display system of Rebar et al because estrogen receptor is one of few nuclear steroid receptors capable of binding ssDNA, which would be necessary for use with M13 phage (also see above). Thus, estrogen and ERE are art recognized as suitable for an intended purpose and according to MPEP 2144.07 "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." (325 U.S. at 335, 65 USPQ at 301.).

One of ordinary skill in the art could have used the estrogen receptor and ERE of Lannigan et al with the phage display system of Rebar et al with a reasonable expectation of success since the estrogen receptor of Lannigan et al is similarly composed of DNA binding Zinc fingers like the protein(s) examined by Rebar et al.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Cull et al 1992 PNAS 89:1865-1869.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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